

**REMARKS**

Claims 1-9 are pending. Claims 10 and 11 are canceled in this Amendment. New claims 19 -20 have been added. No new matter is added through this Amendment.

**Claim Rejections – 35 U.S.C. § 101**

Claims 10-11 are rejected under 35 U.S.C. § 101 as being directed to non-statutory subject matter wherein the claims read on a “product of nature.” In the interest of expediting prosecution and without admitting the propriety of the rejection, the Applicant has canceled Claims 10 and 11 thus removing the rejection.

**Claim Rejections – 35 U.S.C. § 112, First Paragraph**

Claims 1 and 3 (and claims 4 and 5 which depend thereon) are rejected under 35 U.S.C. § 112, first paragraph as containing subject matter not described in the specification in order to reasonably convey to one skilled in the art that the inventor had possession of the claimed invention at the time the application was filed.

Claim 1 has been amended to recite a composition consisting essentially of an isolated shrimp or prawn androgenic polypeptide that is capable of producing a sexually reproductive neomale shrimp or prawn wherein the androgenic polypeptide is derived from a member of the genus *Penaeus* or *Macrobrachium*. New Claim 19 has been added to claim the composition of Claim 1 where the androgenic polypeptide is derived from *Penaeus vannamei* or *Macrobrachium rosenbergii*.

Similarly, Claim 3 has been amended to recite a method of producing a sexually reproductive neomale shrimp or prawn comprising treating a shrimp or prawn with a composition consisting essentially of an androgenic polypeptide to produce a sexually reproductive neomale shrimp or prawn wherein the androgenic polypeptide is derived from a member of the genus *Penaeus* or *Macrobrachium*. Additionally, the term “peptide” in Claim 3 has been replaced with the term “polypeptide” to correct for a typographical error. The term “polypeptide” conforms with the language used in Claim 3 and the other pending claims.

New Claim 20 has been amended to recite a method of producing a sexually reproductive neomale shrimp or prawn comprising treating a shrimp or prawn with a composition consisting essentially of an androgenic polypeptide to produce a sexually reproductive neomale shrimp or prawn wherein the androgenic polypeptide is derived from *Penaeus vannamei* or *Macrobrachium rosenbergii*.

The androgenic polypeptide from *Macrobrachium rosenbergii* and methods of deriving the androgenic polypeptide from *Macrobrachium rosenbergii* are disclosed in Examples 1-4 and 6-7. The androgenic polypeptide from *Penaeus vannamei* and methods of deriving the androgenic polypeptide from *Penaeus vannamei* are disclosed in Example 5-7. One of skill in the art would recognize that the teachings of the Examples can be applied to any species of shrimp from the *Penaeus* genus or any species of prawn from the *Macrobrachium* genus. For example, one of skill in the art would understand that the techniques used to derive the androgenic polypeptide from *Macrobrachium rosenbergii*, Example 1, are equally applicable to other species of prawn encompassed by the *Macrobrachium* genus. Similarly, the techniques outlined in Example 4 for sex-reversal and analysis for *Macrobrachium rosenbergii* are equally applicable to other species of prawn encompassed by the *Macrobrachium* genus.

Furthermore, one of skill in the art would understand that the techniques outlined in Example 5 to derive the androgenic polypeptide from *Penaeus vannamei* and to use the androgenic polypeptide to achieve sex-reversal in *Penaeus vannamei* are equally applicable to other shrimp encompassed by the *Penaeus* genus.

The specification discloses the applicability of the invention to shrimp from the *Penaeus* genus and prawns from the *Macrobrachium* genus on page 6, lines 9-27. The teachings from the Examples in view of the rest of the disclosure would indicate to one of skill in the art that the inventors had possession of the invention as described in the amended claims at the time of filing.

Applicant submits that amended Claims 1 and 3-5 and new Claims 19 and 20 comply with the written description requirement.

**Claim Rejections – 35 U.S.C. § 112, Second Paragraph**

Claim 6 (and claims 7-11 which depend thereon) are rejected under 35 U.S.C. § 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. Claims 10 and 11 have been canceled. The rejection remains for Claims 6-9.

Applicant has amended Claim 6 in compliance with the Examiner's recommendations to recite a skewed percentage of females to males in the steps of the method. Accordingly, Applicant requests that the rejection of Claim 6 (and Claims 7-9 which depend thereon) be withdrawn.

**Claim Rejections – 35 U.S.C. § 102(b) As Being Anticipated by *Malecha, et al.***

Claims 10-11 are rejected under 35 U.S.C. § 102(b) as being as being anticipated by *Malecha, et al.* Applicant respectfully traverses the rejection for reasons of record but has canceled Claims 10-11 in the interest of expediting prosecution.

**Claim Rejections – 35 U.S.C. § 102(b) As Being Anticipated by *Nakashima, et al***

Claims 10-11 are rejected under 35 U.S.C. § 102(b) as being anticipated by *Nakashima, et al.* Applicant respectfully traverses the rejection for reasons of record but has canceled Claims 10-11 in the interest of expediting prosecution.

**Claim Rejections – 35 U.S.C. § 102(b) As Being Anticipated by *EP 0514015***

Claim 2 has been rejected under 35 U.S.C. § 102(b) as being anticipated by EP 0514015. Claim 2 is directed toward neomale shrimp or prawns that are sexually reproductive. The Examiner asserts that EP 0514015 teaches a shellfish that is genotypically female but is phenotypically male. Applicant respectfully traverses the rejection. The techniques used in EP 0514015 to generate a neomale fish have not been shown to successfully generate neomale shrimp or prawns, reproductive or otherwise.

While EP 0514015 purports to be applicable to shellfish, which according to the disclosure of EP 0514015 includes shrimp and prawns, it is widely accepted in the art that inhibition of steroid biosynthesis in female shrimp or prawns will not generate neomales. Instead, as disclosed in the present specification, sexual differentiation in shrimp and prawns is mediated by polypeptide hormones, such as the androgenic polypeptide, rather than the steroid hormones as proposed in EP 0514015. The androgenic polypeptide is peculiar to and specific to crustaceans, such as prawns and shrimp. Applicant has attached a copy of a recent article summarizing the role of androgenic hormones in decapods for support of these arguments (Sagi et al., The Crustacean Androgen: A hormone in an isopod and androgenic activity in decapods, *Amer. Zool.*, 41:477-484 (2001)). Sagi, et al. sets forth five decapod organisms, including *Macrobrachium rosenbergii*, in which it has been demonstrated that the androgenic gland determines sexual differentiation. Sagi, et al., page 479, second column, last paragraph, through page 481, second column, first paragraph and in Table I on page 480. *Macrobrachium rosenbergii* is specifically discussed on page 480, first column, second paragraph, through page 480 second column, first paragraph.

As disclosed in the EU application and as is known in the art, sex reversal in fish can be achieved with a steroid hormone, such as testosterone. The exogenous testosterone applied to sexually immature fish acts like a "fetal" testosterone and masculinizes the sexually immature testes tissue into a functioning testes that in turn produces native testosterone that completes the full masculinization process. In contrast, as shown in the art of record and in the attached Sagi et al. reference, the androgenic polypeptide hormone acts like the "fetal " testosterone and initiates masculinization in crustaceans such as shrimp and prawns. Therefore, one of skill in the art would believe it unlikely that inhibiting estrogen receptors, as described in the EP 0514015, in young sexually immature genetic female shellfish will masculinize them into neomales. Nor would one of skill believe that the administration of steroid hormones would reverse a developing female shrimp or prawn into a neomale.

Applicant further submits that the classification of “shellfish” proposed by EP 0514015 to include crustaceans along with other shellfish is over inclusive and incorrect when discussing the pathways of sexual differentiation.

EP 0514015 provides an extensive list of aromatase inhibitors and provides one example of the use of an aromatase inhibitor to convert a genotypically female fish to phenotypic male fish. Specifically, the Example sets forth the prophetic protocols of exposing fish eggs, fish fry or fry capable of consuming food to various formulations of aromatase inhibitors. The Example does not provide details of the protocols or the outcome of any experiment.

Importantly, while the text of the Example is found almost word for word in the Detailed Description of the Invention, the Example does not mention shellfish at all. Specifically, on page 4, beginning at line 42, the Detailed Description sets forth prophetic protocols for treatment of fish or shellfish eggs. Similarly, on page 5, beginning at line 4, the Detailed Description discloses treatment of hatched fish or fry and hatched shellfish capable of consuming whole food. However, as noted above, the Example omits all reference to shellfish. One of skill reading the Example in view of the Detailed Description would understand that no such experiment had been performed on shellfish.

Furthermore, the specification of EP 0514015 on page 5, lines 24-25 states: “It is anticipated that the same will apply to shellfish.” It is not clear if this statement refers to the entire invention as set forth in EP 0514015 or just to the preceeding paragraph discussing the relationship between body size and reproduction capacity. Either way, it is an indication that fish and shellfish may have different physiological responses to and/or mechanisms of sexual differentiation. These discrepancies in EP 0514015 as between fish and shellfish, in view of the knowledge of those skilled in the art, would lead one to doubt the success of generating neomale shrimp or prawn via the use of aromatase inhibitors.

EP 0514015 does not enable the use of aromatase inhibitors to convert female shrimp or prawns to neomale shrimp or prawns. One of skill in the art would understand that the invention set forth in EP 0514015 would be useful for converting female fish to male fish but would be highly skeptical that the same invention could be successfully practiced on shrimp or prawns. Accordingly, EP 0514015 does not anticipate Claim 2 of the present application.

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Additionally, Claim 2 has been amended to recite a neomale shrimp or prawn wherein the neomale shrimp or prawn was formed from a shrimp or prawn treated with an androgenic polypeptide derived from a member of the genus *Penaeus* or *Macrobrachium*.

Applicant submits that Claim 2 is not anticipated by EP 0514015.

### **Conclusion**

Applicant respectfully submits that the claims are now in condition for allowance. If upon, review, the Examiner feels there are additional outstanding issues, the Examiner is invited to direct any calls in connection with this application to the undersigned at (415) 781-1989.

Respectfully submitted,

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